

General

Guideline Title

Calcium supplementation in pregnant women.

Bibliographic Source(s)

World Health Organization (WHO). Calcium supplementation in pregnant women. Geneva (Switzerland): World Health Organization (WHO); 2013. 30 p. [32 references]

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The definitions for the strength of the recommendations (strong, conditional) are provided at the end of the "Major Recommendations" field.

In populations where calcium intake is low, calcium supplementation as part of the antenatal care is recommended for the prevention of preeclampsia among pregnant women, particularly among those at higher risk of hypertension (*strong recommendation**).

*A strong recommendation is one for which the guideline development group is confident that the desirable effects of adherence outweigh the undesirable effects. Implications of a strong recommendation for patients are that most people in their situation would desire the recommended course of action and only a small proportion would not. Implications for clinicians are that most patients should receive the recommended course of action, and adherence to this recommendation is a reasonable measure of good-quality care. With regard to policy-makers, a strong recommendation means that it can be adapted as a policy in most situations, and for funding agencies it means the intervention likely represents an appropriate allocation of resources (i.e., large net benefits relative to alternative allocation of resources).

Table: Suggested Scheme for Calcium Supplementation in Pregnant Women

Dosage	1.5–2.0 g elemental calcium/day ^a
Frequency	Daily, with the total daily dosage divided into three doses (preferably taken at mealtimes)
Duration	From 20 weeks' gestation until the end of pregnancy
Target group	All pregnant women, particularly those at higher risk of gestational hypertension ^b
Settings	Areas with low calcium intake

^al g of elemental calcium equals 2.5 g of calcium carbonate or 4 g of calcium citrate.

^bWomen are regarded as being at high risk of developing hypertension and pre-eclampsia if they have one or more of the following risk factors: obesity, previous pre-eclampsia, diabetes, chronic hypertension, renal disease, autoimmune disease, nulliparity, advanced maternal age, adolescent pregnancy and conditions leading to hyperplacentation and large placentas (e.g., twin pregnancy). This is not an exhaustive list, but can be adapted/complemented based on the local epidemiology of pre-eclampsia.

Remarks

- Assessment of the risk of developing gestational hypertensive disorders is to be conducted by a clinician. The clinical management of women with pre-eclampsia or eclampsia requires consideration of other evidence-informed interventions.
- Implementation of this recommendation requires close monitoring of women's total daily calcium intake (diet, supplements and antacids). The overall intake of calcium per day should not exceed the locally established upper tolerable limit. In the absence of such reference standards, an upper limit of calcium intake of 3 g/day can be used.
- The mechanisms through which calcium reduces the risk of gestational hypertension need further elucidation. Available evidence supports the theory that calcium supplementation may reduce the risk of developing pre-eclampsia by filling a dietary gap in calcium intake. In populations where consumption of calcium on average meets the recommended dietary calcium intake, either through calcium-rich foods or fortified staple foods, calcium supplementation is not encouraged as it may not improve the outcomes related to pre-eclampsia and hypertensive disorders of pregnancy but might increase the risk of adverse effects. Although antacids are a rich source of calcium, they are not part of the diet and their use should be limited to the treatment of heartburn or indigestion. The calcium content of any other vitamin and mineral supplements that are also being taken should be considered when recommending calcium supplementation, to reduce the risk of hypercalcaemia.
- Determination of the dietary calcium intake of an individual woman is a complex task. The target group for this recommendation comprises
 populations with observed low dietary calcium intake or those living in geographical areas where calcium-rich foods are not commonly
 available or consumed. Calcium intake at population level can be estimated through various means including dietary surveys using 24-hour
 recalls, food frequency questionnaires or food weighing, as well as through secondary data estimates derived from Food and Agriculture
 Organization (FAO) food balance sheets or household consumption and expenditure surveys.
- Healthy dietary practices to promote adequate calcium intake through local calcium-rich foods should be encouraged in the general
 population, including pregnant women.
- Interaction between iron supplements and calcium supplements may occur, although the consequences of prolonged calcium supplementation for iron status among different age groups are still unclear. Therefore, the two nutrients should preferably be administered several hours apart (i.e., iron may be consumed between meals) rather than concomitantly.
- Selection of the most appropriate delivery platform should be context specific, with the aim of reaching the most vulnerable populations and
 ensuring a timely and continuous supply of supplements. Calcium supplementation could be delivered by lay health workers along with
 targeted monitoring and evaluation.
- Calcium supplements are available as tablets or capsules. Tablets (soluble tablets, effervescent tablets, chewable tablets for use in the mouth and modified-release tablets) are solid dosage forms containing one or more active ingredients.

<u>Definitions</u>:

Strong Recommendations

With strong recommendations, the guideline communicates the message that the desirable effects of adherence to the recommendation outweigh the undesirable effects. This means that in most situations the recommendation can be adopted as policy.

Conditional Recommendations

These are made when there is greater uncertainty about the four factors above or if local adaptation has to account for a greater variety in values and preferences, or when resource use makes the intervention suitable for some, but not for other locations. This means that there is a need for substantial debate and involvement of stakeholders before this recommendation can be adopted as policy.

Clinical Algorithm(s)

None provided

Scope

Hypertensive disorders of pregnancy

Guideline Category

Prevention

Clinical Specialty

Obstetrics and Gynecology

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Health Plans

Managed Care Organizations

Physician Assistants

Physicians

Public Health Departments

Utilization Management

Guideline Objective(s)

To provide global, evidence-informed recommendations on calcium supplementation as a public health intervention for the purpose of improving maternal and infant health outcomes

Target Population

- Pregnant women
- Subpopulations (listed in order of priority):
 - Populations with a low versus adequate baseline dietary calcium intake
 - Populations with above average risk versus low or average risk of hypertensive disorders of pregnancy

Interventions and Practices Considered

- 1. Oral calcium supplements
- 2. Oral calcium supplements given in combination with other micronutrients

Major Outcomes Considered

Maternal:

- High blood pressure with or without proteinuria
- High blood pressure with significant proteinuria (pre-eclampsia)

- Eclampsia (the occurrence of one or more convulsions [fits] in association with pre-eclampsia)
- Complications at delivery (assisted delivery)
- Bone softness
- Osteoporosis
- Any adverse effects

Infant:

- Low birth weight (<2500 g)
- Birth weight
- Preterm birth (<37 weeks' gestation)
- · Length at birth
- Admission to a neonatal intensive care unit
- Stillbirth or death in early neonatal period (0–7 days of life)
- Any adverse effects
- Small for gestational age

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse: The World Health Organization (WHO) examined two systematic reviews prepared by The Cochrane Collaboration (see the "Availability of Companion Documents" field).

For both systematic reviews, the review authors searched the Cochrane Pregnancy and Childbirth Group Trials Register by contacting the Trials Search Co-ordinator. For the systemic review on preventing hypertensive disorders, the search date was March 28, 2013 and the search was updated in May 2014 and the results added to studies awaiting classification. For the systemic review on improving pregnancy and infant outcomes, the search date was March 17, 2011.

The Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

- 1. Quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL)
- 2. Weekly searches of MEDLINE
- 3. Weekly searches of EMBASE
- 4. Hand-searches of 30 journals and the proceedings of major conferences
- 5. Weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts

For both systematic reviews, details of the search strategies for CENTRAL, MEDLINE and EMBASE, the list of hand-searched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the "Specialized Register" section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

For details of searches carried out in the previous version of the systemic review on preventing hypertensive disorders, see Appendix 1 in the systematic review document (see the "Availability of Companion Documents" field).

No language restrictions were applied for either systematic review.

Please see the systematic reviews for the criteria for considering studies, including types of studies, types of participants, types of interventions and types of outcome measures (see the "Availability of Companion Documents" field).

Number of Source Documents

Calcium Supplementation During Pregnancy for Preventing Hypertensive Disorders and Related Problems

The search strategy identified 49 studies, of which 24 were included. Seven trial reports are awaiting classification.

Calcium Supplementation (Other Than for Preventing or Treating Hypertension) for Improving Pregnancy and Infant Outcomes

The search yielded 72 trial reports. After exploring the contents, and grouping for the same study, the review authors included data from 21 trials (54 reports).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group Grades of Evidence

High quality: The Working Group is very confident that the true effect lies close to that of the estimate of the effect.

Moderate quality: The Working Group has moderate confidence in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low quality: The Working Group's confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.

Very low quality: The Working Group has very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of the effect.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse: The World Health Organization (WHO) examined two systematic reviews prepared by The Cochrane Collaboration (see the "Availability of Companion Documents" field).

Data Extraction and Management

Calcium Supplementation During Pregnancy for Preventing Hypertensive Disorders and Related Problems

The Cochrane Collaboration designed a form to extract data. They resolved discrepancies through discussion. They entered data into Review Manager software (RevMan 2012) and checked it for accuracy.

When study information and/or data were unclear, they attempted to contact authors of the original reports to provide further details.

Calcium Supplementation (Other Than for Preventing or Treating Hypertension) for Improving Pregnancy and Infant Outcomes

Two Cochrane Collaboration review authors designed a form to extract data. For eligible studies, they extracted the data using the agreed form.

They resolved discrepancies through discussion and consulted other review authors if necessary. The authors entered data into Review Manager software (RevMan 2011) and checked for accuracy. When information on any studies was unclear, they attempted to contact authors of the original reports to provide further details.

Assessment of Risk of Bias in Included Studies

Calcium Supplementation During Pregnancy for Preventing Hypertensive Disorders and Related Problems

Two review authors independently assessed risk of bias for each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions. They resolved any disagreement by discussion or by involving a third assessor. See the systematic review document for more information.

Calcium Supplementation (Other Than for Preventing or Treating Hypertension) for Improving Pregnancy and Infant Outcomes

Two review authors assessed the validity of each study independently using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions. See the systematic review document for more information.

Data Synthesis

Calcium Supplementation During Pregnancy for Preventing Hypertensive Disorders and Related Problems

The Cochrane Collaboration carried out statistical analysis using the Review Manager software (RevMan 2012). They used fixed-effect metaanalysis for combining data where it was reasonable to assume that studies were estimating the same underlying treatment effect (i.e., where trials
were examining the same intervention, and the trials' populations and methods were judged sufficiently similar). If there was clinical heterogeneity
sufficient to expect that the underlying treatment effects differed between trials, or if substantial statistical heterogeneity was detected, they used
random-effects meta-analysis to produce an overall summary, if an average treatment effect across trials was considered clinically meaningful. The
random-effects summary was treated as the average of the range of possible treatment effects and the review authors discussed the clinical
implications of treatment effects differing between trials. If the average treatment effect was not clinically meaningful, they did not combine trials.
When they used random-effects analyses, the results are presented as the average treatment effect with its 95% confidence interval, and the
estimates of $Tau(T)^2$ and $Tau(T)^2$ a

Calcium Supplementation (Other Than for Preventing or Treating Hypertension) for Improving Pregnancy and Infant Outcomes

The Cochrane Collaboration carried out statistical analysis using the Review Manager software (RevMan 2011). They used fixed-effect meta-analysis for combining data where it was reasonable to assume that studies were estimating the same underlying treatment effect: i.e., where trials were examining the same intervention, and the trials' populations and methods were judged sufficiently similar. When there was clinical heterogeneity sufficient to expect that the underlying treatment effects would differ between trials, or when substantial statistical heterogeneity was detected, they used random-effects meta-analysis to produce an overall summary provided that an average treatment effect across trials was considered clinically meaningful. They treated the random-effects summary as the average range of possible treatment effects and discussed the clinical implications of treatment effects differing between trials. When they considered that an average treatment effect was not clinically meaningful they did not combine trials.

When they used random-effects analyses, they presented the summary result as the average treatment effect with its 95% confidence interval, and with the estimates of T^2 and I^2 .

Subgroup Analysis and Investigation of Heterogeneity

Calcium Supplementation During Pregnancy for Preventing Hypertensive Disorders and Related Problems

When the Cochrane Collaboration identified substantial heterogeneity, the review authors investigated it using subgroup analyses. They considered whether an overall summary was meaningful, and if it was, used random-effects analysis to produce it.

They carried out the following subgroup analyses.

- 1. Trials in populations with low versus adequate dietary calcium intake
- 2. Trials in participants with low/average versus high hypertensive risk
- 3. Trials with small versus larger sample sizes

They used only primary outcomes in subgroup analyses 2 and 3. The review authors assessed subgroup differences by interaction tests available within RevMan (RevMan 2012). They reported the results of subgroup analyses quoting the Chi^2 statistic and P value, and the interaction test I^2

value.

Calcium Supplementation (Other Than for Preventing or Treating Hypertension) for Improving Pregnancy and Infant Outcomes

When The Cochrane Collaboration identified substantial heterogeneity, they investigated it using subgroup analyses and sensitivity analyses.

They carried out the following subgroup analyses:

- 1. Total dose per day of calcium supplementation: low/high (less than 1000 and 1000 or more mg)
- 2. Time supplementation taken during pregnancy (the time that calcium supplementation started)
 - First half of pregnancy (less than 20 weeks)
 - Second half of pregnancy (20 weeks or more)
- 3. Type of calcium supplementation preparation; calcium carbonate, lactate, gluconate

They used the following outcomes in subgroup analysis:

- Preterm birth less than 37 weeks
- Low birth weight (less than 2500 g)

They assessed differences between subgroups by inspection of the subgroups' confidence intervals; non-overlapping confidence intervals suggesting a statistically significant difference in treatment.

Sensitivity Analysis

Calcium Supplementation During Pregnancy for Preventing Hypertensive Disorders and Related Problems

The review authors undertook sensitivity analysis by considering the results of the larger sample size trials versus the overall results for primary outcomes.

For more information on data collection and analysis for both systematic reviews, including assessment of risk of bias in included studies, see the systematic review documents (see the "Availability of Companion Documents" field).

Calcium Supplementation (Other Than for Preventing or Treating Hypertension) for Improving Pregnancy and Infant Outcomes

The review authors carried out sensitivity analyses to explore the effect of trial quality based on concealment of allocation. They excluded trials rated as "high risk of bias" or "unclear risk of bias" for allocation concealment in order to assess for any substantive difference to the overall result.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

This guideline was developed in accordance with the World Health Organization (WHO) evidence-informed guideline development procedures, as outlined in the WHO handbook for guideline development (see the "Availability of Companion Documents" field).

Scope of the Guideline, Evidence Appraisal and Decision-making

An initial set of questions (and the components of the questions) to be addressed in the guideline was the critical starting point for formulating the recommendation. The questions were drafted by technical staff at the Evidence and Programme Guidance Unit, Department of Nutrition for Health and Development, based on policy and programme guidance needs of Member States and their partners. The population, intervention, control, outcomes (PICO) format was used (see Annex 7 in the original guideline document). The questions were discussed and reviewed by the WHO Steering Committee for Nutrition Guidelines Development, and feedback was received from four stakeholders.

A Nutrition Guidance Advisory Group meeting was held on 14–16 March 2011 in Geneva, Switzerland, to finalize the scope of the questions and rank the critical outcomes and populations of interest for the recommendation on calcium supplementation in pregnant women for the improvement of maternal and neonatal outcomes. The Nutrition Guidance Advisory Group–Micronutrients Subgroup discussed the relevance of the questions and modified them as needed. The guideline group scored the relative importance of each outcome from 1 to 9 (where 7–9 indicated that the outcome was critical for a decision, 4–6 indicated that it was important and 1–3 indicated that it was not important). The final key questions on this

intervention, along with the outcomes that were identified as critical for decision-making, are listed in PICO format in Annex 7 in the original guideline document.

Two systematic reviews were used to summarize and appraise the evidence using the Cochrane methodology for randomized controlled trials* (see the "Availability of Companion Documents" field). WHO staff prepared evidence summaries according to the *Grading of Recommendations Assessment, Development and Evaluation* (GRADE) approach to assess the overall quality of the evidence. GRADE considers: the study design; the limitations of the studies in terms of their conduct and analysis; the consistency of the results across the available studies; the directness (or applicability and external validity) of the evidence with respect to the populations, interventions and settings where the proposed intervention may be used; and the precision of the summary estimate of the effect.

Both the systematic reviews and the GRADE evidence profiles for each of the critical outcomes were used for drafting this guideline. The draft recommendation was discussed by the WHO Steering Committee for Nutrition Guidelines Development and at a second consultation with the Nutrition Guidance Advisory Group, held on 7–9 November 2011 in Washington DC, United States of America. At the second consultation, the guideline development group members independently voted on the strength of the recommendation, taking into account: (i) the desirable and undesirable effects of the intervention; (ii) the quality of the available evidence; (iii) values and preferences related to the intervention in different settings; and (iv) the cost of options available to health-care workers in different settings (see Annex 3 in the original guideline document). It was noted how they balanced the decisions for each of the four domains. The voting results and the summary of the considerations for establishing the strength of the recommendation were disclosed before the end of the meeting and further discussed as needed. Consensus was defined as agreement by simple majority of the guideline group members. WHO staff present at the meeting as well as other external technical experts involved in the collection and grading of the evidence were not allowed to vote. There were no strong disagreements among the guideline group members.

Summary of the Nutrition Guidance Advisory Group's Considerations for Determining the Strength of the Recommendation

Quality of evidence:	 Low and moderate-quality evidence for most outcomes Clear impact on pre-eclampsia and possibly on preterm birth Low-quality evidence for adverse effects
Values and preferences:	 Effects greater in those with low calcium intake and larger doses of calcium Evidence is consistent for pre-eclampsia and preterm birth, both of which are responsible for a considerable proportion of the burden of maternal and infant morbidity and mortality Some members noted that the two largest studies do not show a clinical impact of this intervention
Trade-off between benefits and harms:	 Current evidence suggests that benefits outweigh disadvantages, particularly in populations with low calcium intake The possibility of developing haemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome, and renal stones is a concern and more evidence is needed for this outcome
Costs and feasibility:	 This intervention may be adopted as a policy when adequate health systems and delivery platforms already exist There is a lack of information on the cost of this intervention This intervention may require intensive resources to target those women with an increased risk of hypertension

Rating Scheme for the Strength of the Recommendations

Strong Recommendations

With strong recommendations, the guideline communicates the message that the desirable effects of adherence to the recommendation outweigh the undesirable effects. This means that in most situations the recommendation can be adopted as policy.

Conditional Recommendations

These are made when there is greater uncertainty about the four factors above or if local adaptation has to account for a greater variety in values and preferences, or when resource use makes the intervention suitable for some, but not for other locations. This means that there is a need for substantial debate and involvement of stakeholders before this recommendation can be adopted as policy.

Cost Analysis

The guideline developers reviewed a published cost analysis.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The External Experts and Stakeholders Panel (see Annex 6 in the original guideline document) was consulted on the scope of the guideline, the questions addressed and the choice of important outcomes for decision-making, as well as with regard to review of the completed draft guideline. This was done through the World Health Organization (WHO) Micronutrients and Standing Committee on Nutrition (SCN) mailing lists that together included over 5500 subscribers, and through the WHO nutrition web site

A public call for comments on the final draft guideline was released in 2012. All interested stakeholders became members of the External Experts and Stakeholders Panel but were allowed to comment on the draft guideline only after submitting a signed Declaration of Interests form. Feedback was received from 46 stakeholders. WHO staff addressed each comment and then finalized the guideline and submitted it for clearance by WHO before publication.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for the recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Potential to reduce adverse gestational outcomes, in particular by decreasing the risk of developing hypertensive disorders during pregnancy, which are associated with a significant number of maternal deaths and considerable risk of preterm birth

Potential Harms

Women who received calcium supplements had a significantly higher risk of developing haemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome, a rare adverse event associated with severe pre-eclampsia

Qualifying Statements

Qualifying Statements

- The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization (WHO) concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.
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Implementation of the Guideline

Description of Implementation Strategy

Adaptation and Implementation

As this is a global guideline it should be adapted to the context of each Member State. Prior to implementation, a public health programme that includes the provision of calcium supplements to pregnant women should have well-defined objectives that take into account available resources, existing policies, suitable delivery platforms and suppliers, communication channels, and potential stakeholders. Ideally, calcium supplementation should be implemented as part of an integrated programme for antenatal care and preceded by an assessment of the calcium intake at population level. The latter can be estimated through various means including dietary surveys using 24-hour recalls, food frequency questionnaires or food weighing, as well as through secondary data estimates derived from Food and Agriculture Organization (FAO) food balance sheets or household consumption and expenditure surveys.

To ensure that World Health Organization (WHO) global guidelines and other evidence-informed recommendations for nutrition interventions are better implemented in low and middle-income countries, the Department of Nutrition for Health and Development works with the WHO Evidence-Informed Policy Network (EVIPNet) programme. EVIPNet promotes partnerships at country level between policy-makers, researchers and civil society to facilitate policy development and implementation through use of the best available evidence.

Monitoring and Evaluation of Guideline Implementation

A plan for monitoring and evaluation with appropriate indicators is encouraged at all stages. The impact of this guideline can be evaluated within countries (i.e., monitoring and evaluation of the programmes implemented at national or regional scale) and across countries (i.e., the adoption and adaptation of the guideline globally). The WHO Department of Nutrition for Health and Development, Evidence and Programme Guidance Unit, jointly with the Centers for Disease Control and Prevention (CDC) International Micronutrient Malnutrition Prevention and Control (IMMPaCt) programme, and with input from international partners, has developed a generic logic model for micronutrient interventions in public health to depict the plausible relationships between inputs and expected MDGs by applying the micronutrient programme evaluation theory. Member States can adjust the model and use it in combination with appropriate indicators, for designing, implementing, monitoring and evaluating the successful escalation of nutrition actions in public health programmes.

For evaluation at the global level, the WHO Department of Nutrition for Health and Development has developed a centralized platform for sharing information on nutrition actions in public health practice implemented around the world. By sharing programmatic details, specific country adaptations and lessons learnt, this platform will provide examples of how guidelines are being translated into nutrition actions.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Staying Healthy

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

World Health Organization (WHO). Calcium supplementation in pregnant women. Geneva (Switzerland): World Health Organization (WHO); 2013. 30 p. [32 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013

Guideline Developer(s)

World Health Organization - International Agency

Source(s) of Funding

World Health Organization (WHO) thanks the Government of Luxembourg for financial support for this work.

Guideline Committee

World Health Organization (WHO) Steering Committee for Nutrition Guidelines Development

Composition of Group That Authored the Guideline

Members of the Nutrition Guidance Advisory Group – Micronutrients: Ms Deena Alasfoor, Ministry of Health, Muscat, Oman, health programme management, food legislations, surveillance in primary health care; Dr Beverley-Ann Biggs, International and Immigrant Health Group, Department of Medicine, University of Melbourne, Parkville, Australia, micronutrients supplementation, clinical infectious diseases; Dr Héctor Bourges Rodríguez, Instituto Nacional de Ciencias Medicas y Nutrición Salvador Zubiran, Mexico City, Mexico, nutritional biochemistry and metabolism research, food programmes, policy, and regulations; Dr Norm Campbell, Departments of Medicine Community Health Sciences and Physiology and Pharmacology, University of Calgary, Calgary, Canada, physiology and pharmacology, hypertension, prevention and control; Dr Rafael Flores-Ayala, Centers for Disease Control and Prevention (CDC), Atlanta, United States of America, nutrition and human capital formation, nutrition and growth, impact of micronutrient interventions; Engineer Wisam Qarqash, Jordan Health Communication Partnership, Johns Hopkins University, Bloomberg School of Public Health, Amman, Jordan, design, implementation and evaluation of health communications and programmes; Dr Daniel Raiten, Office of Prevention Research and International Programs, National Institutes of Health (NIH) Bethesda, United States of America, malaria, maternal and child health, human development research; Dr Mahdi Ramsan Mohamed, Research Triangle Institute (RTI) International, Dar es Salaam, the United Republic of Tanzania, malaria control and prevention, neglected tropical diseases; Dr Meera Shekar, Health Nutrition Population, Human Development Network (HDNHE), The World Bank, Washington, DC, United States of America, costing of interventions in public health nutrition, programme implementation; Dr Rebecca Joyce Stoltzfus, Division of Nutritional Sciences, Cornell University Ithaca, United States of America, International nutrition and public health, iron and vitamin A nutri

Malik Goonewardene, Department of Obstetrics and Gynaecology, University of Ruhuna, Galle, Sri Lanka, obstetrics and gynaecology, clinical practice; Dr Junsheng Huo, National Institute for Nutrition and Food Safety, Chinese Center for Disease Control and Prevention, Beijing, China, food fortification, food science and technology, standards and legislation; Dr Janet C. King, Children's Hospital Oakland, Research Institute, Oakland, United States of America, micronutrients, maternal and child nutrition, dietary requirements; Dr Marzia Lazzerini, Department of Paediatrics and Unit of Research on Health Services and International Health Institute for Maternal and Child Health, IRCCS Burlo Garofolo, Trieste, Italy, paediatrics, malnutrition, infectious diseases; Professor Malcolm E. Molyneux, College of Medicine — University of Malawi, Blantyre, Malawi Malaria, international tropical diseases research and practice; Ms Carol Tom, East, Central and Southern Africa Health Community (ECSA-HC), Nairobi, Kenya, food fortification technical regulations and standards, policy harmonization; Dr David Tovey, The Cochrane Library, Cochrane Editorial Unit, London, England, systematic reviews, health communications, evidence for primary health care; Mrs Vilma Qahoush Tyler, UNICEF Regional Office for Central and Eastern Europe and the Commonwealth of Independent States (CEE/CIS), Geneva, Switzerland, food fortification, public health programmes; DrGunn Elisabeth Vist, Department of Preventive and International Health Norwegian Knowledge Centre for the Health Services, Oslo, Norway, systematic review methods and evidence assessment using GRADE methodology; Dr Emorn Wasantwisut, Mahidol University, Nakhon Pathom, Thailand, international nutrition, micronutrient biochemistry and metabolism

Members of the WHO Steering Committee for Nutrition Guidelines Development: Dr Ala Alwan, Acting Director, Department of Chronic Diseases and Health Promotion, Noncommunicable Diseases and Mental Health (NMH) Cluster; Dr Francesco Branca, Director, Department of Nutrition for Health and Development, Noncommunicable Diseases and Mental Health (NMH) Cluster; Dr Ruediger Krech, Director, Department of Ethics, Equity, Trade and Human Rights Information, Evidence and Research (IER) Cluster; Dr Knut Lonnroth, Medical Officer, The Stop TB Strategy, HIV/AIDS, TB and Neglected Tropical Diseases (HTM) Cluster; Dr Daniel Eduardo Lopez Acuña, Director, Department of Strategy, Policy and Resource Management, Health Action in Crises (HAC) Cluster; Dr Elizabeth Mason, Director, Department of Maternal, Neonatal, Child and Adolescent Health and Development Family and Community Health (FCH) Cluster; Dr Michael Mbizvo, Director, Department of Reproductive Health and Research, Family and Community Health (FCH) Cluster; Dr Jean-Marie Okwo-Bele, Director, Department of Immunization, Vaccines and Biologicals, Family and Community Health (FCH) Cluster; Dr Gottfried Otto Hirnschall, Director, Department of HIV/AIDS, HIV/AIDS, TB and Neglected Tropical Diseases (HTM) Cluster; Dr Isabelle Romieu, Director, Dietary Exposure Assessment Group, Nutrition and Metabolism Section, International Agency for Research on Cancer (IARC), Lyons, France; Dr Sergio Spinaci, Associate Director, Global Malaria Programme, HIV/AIDS, TB and Neglected Tropical Diseases (HTM) Cluster; Dr Willem Van Lerberghe, Director, Department of Food Safety, Zoonoses and Foodborne Diseases, Health Security and Environment (HSE) Cluster; Dr Nevio Zagaria, Acting Director, Department of Emergency Response and Recovery Operations, Health Action in Crises (HAC) Cluster

Financial Disclosures/Conflicts of Interest

According to the rules in the World Health Organization (WHO) Basic documents , all experts participating in WHO meetings must declare any interest relevant to the meeting prior to their participation. The conflicts of interest statements for all guideline group members were reviewed by the responsible technical officer and the relevant departments before finalization of the group composition and invitation to attend a guideline group meeting. All guideline group members and participants of the guideline development meetings submitted a Declaration of Interests form along with their curriculum vitae before each meeting. In addition, they verbally declared potential conflicts of interest at the beginning of each meeting. The procedures for management of conflicts of interest strictly followed WHO *Guidelines for declaration of interests (WHO experts)*. The potential conflicts of interest declared by the members of the guideline group are summarized below.

- Dr Héctor Bourges Rodriguez declared being chair of the executive board of the Danone Institute in Mexico, a non-profit organization promoting research and dissemination of scientific knowledge in nutrition, and receiving funds as chair honorarium from this organization. Some activities of the Danone Institute in Mexico may generally relate to nutrition and are funded by Danone Mexico, a food producer.
- Dr Emorn Wasantwisut declared serving as a technical/scientific adviser to the International Life Sciences Institute (ILSI)/South East Asia's
 Food and Nutrients in Health and Disease Cluster and as a reviewer of technical documents and speaker for Mead Johnson Nutritionals.
 Her research unit received funds for research support from Sight and Life and the International Atomic Energy Agency for the use of stable isotopes to define interactions of vitamin A and iron.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the World Health Organization (WHO) Web site

Print copies: Available from the WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland; Phone: +41 22 791 3264; Fax: +41 22 791 4857; E-mail: bookorders@who.int

Availability of Companion Documents

copies: Available from The Cochrane Library Web site

The following are available:

•	Buppasiri P, Lumbiganon P, Thinkhamrop J, Ngamjarus C, Laopaiboon M. Calcium supplementation (other than for preventing or treating
	hypertension) for improving pregnancy and infant outcomes (review). Cochrane Database of Systematic Reviews 2011, Issue 10. Art. No
	CD007079. 2011. 95 p. Electronic copies: Available from The Cochrane Library Web site
•	Hofmeyr GJ, Lawrie TA, Atallah AN, Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders and
	related problems (review). Cochrane Database of Systematic Reviews 2014, Issue 8. Art. No.: CD001059. 2014. 132 p. Electronic

• World Health Organization. WHO handbook for guideline development. Geneva (Switzerland): World Health Organization (WHO); 2012. 63 p. Electronic copies: Available from the World Health Organization (WHO) Web site

Patient Resources

None available

NGC Status

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